REMARKS

Claims 1-24, 26-36, 38-42, and 43-55 are currently pending in this application after entry of the instant response. Claims 25 and 37 have been cancelled without prejudice. Claim 47 is withdrawn from consideration. Claims 1-24, 26-36, 38-46 and 48-55 have been rejected. Applicants reserve the right to file a continuing application directed to the withdrawn and/or cancelled claims which continuing application is entitled to priority of the present application.

Claim 26 has been amended to depend from claim "22". No new matter has been introduced with this amendment. Support can be found throughout the instant specification and claims as filed.

Claims 34 and 35 have been amended to depend from claim "32" for antecedent purposes. No new matter has been introduced with this amendment. Support can be found throughout the instant application, for example on page 10 (second full paragraph) – page 11 (line 2) as filed.

Claim 44 has been amended to depend from claim "40" and to replace the phrase "ligand is biotin" with "capture sequence probe is biotinylated" for clarity. No new matter has been introduced with this amendment. Support can be found throughout the instant application and the original claims as filed.

Claims 56 and 57 have been added as new claims. No new matter has been introduced with this amendment. Support can be found throughout the instant specificaiton and claims, for example in Example 3 of the application as filed.

Reconsideration and withdrawal of the pending rejections is respectfully requested in view of the remarks submitted herein.

Response to Rejections under 35 U.S.C. §112

Claims 34-35 have been rejected under 35 U.S.C. §112, second paragraph as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Examiner contends that there is insufficient antecedent basis for the phrase "the solid [phase]" in these claims or claim 22 from which they depend. Applicants have amended claims 34-35 to depend from claim 32 which contains the element "a solid phase." Applicants assert that the amended claims now have antecedent support for the phrase "the solid phase."

Applicants believe that the above mentioned amendments address the Examiner's concerns and respectfully request reconsideration and withdrawal of the 35 U.S.C. §112 rejection to claims 34-35.

Response to Rejections under 35 U.S.C. §102(b)

The Examiner has rejected claims 22-23, 31, 36, 40-41, and 42 under 35 U.S.C. § 102(b) for allegedly being anticipated by Mazzulli, *et al.* (*J. Clinical Microbiol.* Vol. 37, No. 4, pages 958-963 April 1999) ("Mazzulli"). Specifically, the Examiner takes the position that Mazzulli teaches "hybridizing a single-stranded target nucleic acid to a capture sequence probe (carrier DNA) and an unlabeled signal sequence probe" (May 1, 2007 Office Action at page 3). The Examiner thus equates the capture sequence probe of the pending claims with the carrier DNA utilized by Mazzulli. Applicants respectfully disagree and submit that the carrier DNA of Mazzulli cannot properly be equated with the capture sequence probe of the pending claims, and that the Examiner's rejection of the pending claims based on Mazzulli should be withdrawn.

Mazzulli describes the use of a positive calibrator comprising CMV plasmid and carrier DNA, and a negative calibrator comprising carrier DNA but no CMV plasmid. These

negative and positive calibrators, as well as the specimens, were treated identically as described on page 959, first full paragraph, lines 20-32. Within the art, "carrier DNA" is commonly used to reduce the loss of sample DNA by non-specific binding to non-biological surfaces, especially where the sample DNA is in low concentration or amount. For example, Hara et al. ("Small Sample Whole-Genome Amplification", Optics East 2005, UCRL-PROC-216415, Lawrence Livermore National Laboratory, October 21, 2005; submitted herewith) explains, in Section 2.2.2, the character and purpose of carrier DNA:

> Carrier DNA, such as salmon sperm DNA, was the next candidate examined for increasing productivity yield from small starting samples. Salmon sperm DNA has been used to reduce background noise in Fluorescent In-Situ Hybridization (FISH). The reduction in background noise is thought to be caused by the carrier DNA's affinity for nonbiological surfaces, such as the sides of a microfuge tube. Carrier DNA is added to the MDA reaction mixture prior to the template DNA to allow time for the coating of non-biological surfaces, such as the sides of a microfuge tube. Thus, the non-specific binding of precious DNA template molecules can be eliminated. (emphasis added; citations omitted).

Similarly, Brigotti, *et al.* (*Nucleic Acids Res.*, Vol. 26, No. 18, pp 4306-4307, 1998; submitted herewith) describe the use of carrier DNA (at p. 4306, col. 2, 2nd complete paragraph, lines 1-6) to avoid losses in the substrate DNA used in an analytical assay due to a centrifugation step ("Incubation of trace amounts of the substrate (20 ng) in the conditions of the polynucleotide:adenosine glycosidase assay (pH 4.0, 40 min at 30°C, see below) showed that most of the radioactivity [signal] was lost upon centrifugation unless carrier salmon sperm DNA was added"; emphasis added).

Thus, carrier DNA is understood in the art as a useful means for reducing the binding of target DNA to non-biological surfaces, presumably by non-specifically binding to such non-biological surfaces and thereby occupying non-specific binding sites to the exclusion of target DNA which is allowed to remain in solution where it can be detected or otherwise treated.

By its very nature, carrier DNA is non-specific, it is intended to bind to non-biological surfaces, and it is not intended to hybridize with target DNA. Mazzulli does not disclose that the carrier DNA used in the calibrators is anything other than carrier DNA as commonly understood in the art. Moreover, Mazzulli does not disclose that the carrier DNA in the calibrators hybridizes to the single-stranded target nucleic acid, forms double-stranded hybrids, hybridizes with blocker probes, or allow for capturing of the capture sequence probe:target portion of the hybrid complex. Mazzulli's use of carrier DNA cannot properly be equated with the use of capture sequence probes in the pending claims.

In addition, Mazzulli's carrier DNA in the calibrators allows for handling small amounts of CMV plasmid in the positive calibrator. To have a proper corresponding negative control, the negative calibrator also contains carrier DNA but no CMV plasmid DNA. The carrier DNA is not present in any other part of the assay described by Mazzulli and is not present in the assay of the actual samples. Indeed, if the carrier DNA functioned as a capture sequence probe, then it would be included in the specimen assay portion, as opposed to only in the calibration assay portion. Therefore, the carrier DNA described by Mazzulli is not the same, in either form or function, as the capture sequence probe of the instant claims.

Moreover, Mazzulli does not disclose a method which comprises hybridizing a single-stranded target nucleic acid to a capture sequence probe and an unlabeled signal sequence probe, "wherein the capture sequence probe and the signal sequence probe hybridizes to non-overlapping regions within the target nucleic acid and do not hybridize to each other" as claimed in the instant invention. According to MPEP §2131, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a

single prior art reference." Therefore, Mazzulli does not anticipate the instant invention, because Mazzulli does not teach each and every element of the invention.

Applicants respectfully request the reconsideration and withdrawal of the 35 U.S.C. § 102(b) rejections to claims 22-23, 31, 36, 40-41, and 42 in view of the aforementioned remarks.

Response to Rejections under 35 U.S.C. §103(a)

Claims 24, 26-27, 34-35, and 43-45 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Mazzulli in view of Brakel, *et al.* (USPN: 5,082,830) ("Brakel"). The Examiner cites Brakel for utilizing biotin labeled nucleotides "in detection of the target by combining with a streptavidin for enhancing the signal reporting moiety" (Office Action, page 5). The applicants respectfully disagree and traverse the rejection to these claims because the combination of Brakel with Mazzulli does not result in the instant invention.

The applicants respectfully direct the Examiner's attention to MPEP § 2143.03 which states: "To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." As described previously, in the "Response to Rejections under 35 U.S.C. §102(b)", Mazzulli does not disclose a method which comprises hybridizing a single-stranded target nucleic acid to a capture sequence probe and an unlabeled signal sequence probe, "wherein the capture sequence probe and the signal sequence probe hybridizes to non-overlapping regions within the target nucleic acid and do not hybridize to each other" as claimed in the instant invention. Additionally, the Examiner admits that Mazzulli "did not teach labeling capture probe with biotin labels at each of the 5' and 3' ends of the probe, and binding with streptavidin" (Office Action, page 5). The applicants assert that the

deficiencies of Mazzulli, are not overcome by Brakel. Neither Mazzulli nor Brakel, alone or in combination, teach or suggest all of the aspects of the instant invention. Specifically, neither Mazzulli nor Brakel, teach or suggest:

> [a] method of detecting a target nucleic acid comprising… hybridizing a single-stranded target nucleic acid to a capture sequence probe and an unlabeled signal sequence probe, wherein the capture sequence probe and the signal sequence probe hybridizes to non-overlapping regions within the target nucleic acid and do not hybridize to each other…

Therefore, the combination of Mazzulli with Brakel do not render the claims obvious.

Applicants respectfully request the withdrawal of the 35 U.S.C. §103(a) rejection to claims 24, 26-27, 34-35, and 43-45 in view of the aforementioned remarks.

Claims 28-30 and 33 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Mazzulli in view of Collins, *et al.* ("Collins") (USPN: 5,750,338). The Examiner cites Collins for allegedly teaching a method that comprises:

> (i) the capture sequence probe and signal sequence probe hybridize to regions of the target nucleic acid comprising less than 500 bases apart (see col. 19, line 32-38); (ii) comprises forming single-stranded DNA prior to hybridization (see col. 29, line 10[-]33, table 4, step 1, indicating denaturation step); and (iii) hybridization is carried out at room temperature (see col. 28, line 9-17) (Office Action, page 6).

The applicants respectfully disagree with the Examiner's contentions and traverse this rejection.

The applicants respectfully direct the Examiner's attention to MPEP § 2143.03 which states: "To establish *prima facie* obviousness of a claimed invention, all the claim

limitations must be taught or suggested by the prior art." As described previously, in the "Response to Rejections under 35 U.S.C. §102(b)", Mazzulli does not disclose a method which comprises hybridizing a single-stranded target nucleic acid to a capture sequence probe and an unlabeled signal sequence probe, "wherein the capture sequence probe and the signal sequence probe hybridizes to non-overlapping regions within the target nucleic acid and do not hybridize to each other" as claimed in the instant invention. Additionally, the Examiner admits that Mazzulli "did not teach the hybridizing distance between the hybridizing probes on the target, dentaturing the target before hybridization, and hybridization conditions" (Office Action, page 6). The applicants assert that the deficiencies of Mazzulli, are not overcome by Collins. Neither Mazzulli nor Collins, alone or in combination, teach or suggest all of the aspects of the instant invention. Specifically, neither Mazzulli nor Collins, teach or suggest:

> [a] method of detecting a target nucleic acid comprising… hybridizing a single-stranded target nucleic acid to a capture sequence probe and an unlabeled signal sequence probe, wherein the capture sequence probe and the signal sequence probe hybridizes to non-overlapping regions within the target nucleic acid and do not hybridize to each other…

Therefore, the combination of Mazzulli with Collins do not render the claims obvious.

Applicants respectfully request the withdrawal of the 35 U.S.C. §103(a) rejection to claims 28-30 and 33 in view of the aforementioned remarks.

Response to Non-Statutory Double Patenting Rejection

Claims 1-24, 26-36, 38-46, and 48-55 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-52 and 54-92 of copending Application No. 10/311,645 (Publn. No. US 2004/0214302). Since the

conflicting claims have not in fact been patented, this is a provisional obviousness-type double patenting rejection.

In response, applicants respectfully request that the provisional double-patenting rejection be held in abeyance due to the provisional nature of the rejection until one of the applications is allowed. Upon notice of otherwise allowable subject matter, applicants will address the rejection. Applicants note that it is proper when dealing with otherwise allowable subject matter in co-pending applications to withdraw a provisional rejection in the most advanced application, allow it to issue, and make a (non-provisional) rejection in the remaining application.

Thus, applicants respectfully submit that the claims as presented herein are allowable over the art of record, and respectfully request that the respective rejections and objections be withdrawn.

Dependent Claims

Applicants have not independently addressed all of the rejections of the dependent claims. Applicants submit that for at least similar reasons as to why independent claims 1, 2, 22, 40, and 50 from which all of the dependent claims depend are believed allowable as discussed supra, the dependent claims are also allowable. Applicants however, reserve the right to address any individual rejections of the dependent claims and present independent bases for allowance for the dependent claims should such be necessary or appropriate.

Thus, applicants respectfully submit that the invention as recited in the claims as presented herein is allowable over the art of record, and respectfully request that the respective rejections and objections be withdrawn.

CONCLUSION

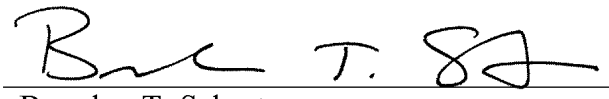
Based on the foregoing amendments and remarks, applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application. Applicants respectfully believe that the subject application is patentably distinguished over the art and that the claims are in condition for allowance. An action passing this case to issue is courteously urged.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **13-4500**, Order No. 2629-4017.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **13-4500**, Order No. 2629-4017.

Respectfully submitted,
MORGAN & FINNEGAN, L.L.P.

Dated: September 4, 2007 By: 

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